Citation:

Little RE, Northstone K, Golding J, ALSPAC Study Team. Alcohol, breastfeeding, and development at 18 months. *Pediatrics*. 2002; May:109(5):E72-2.

PubMed ID: <u>11986478</u>

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:



POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The aim of this study was to determine if a mother's regular consumption of alcohol while nursing affects the infant's motor development.

Inclusion Criteria:

- The sample for this study was drawn from the Children in Focus cohort
 - Children who completed the Griffiths Scales of Mental Development at 18 months with all parts completed
 - Information available on the usual alcohol consumption and alcohol binges in the postpartum period
 - Information available on the length of lactation and timing of supplementation in the first 3 months after birth
 - Mothers enrolled by the end of the sixth month of pregnancy
 - Birth of a singleton and at least 34 weeks gestation
- Informed consent is obtained annually and separate consent is obtained in advance for each specific Children in Focus procedure

Exclusion Criteria:

- Pregnant women outside of the defined area in Avon County, United Kingdom
- Expected delivery date before April 1, 1991 or after December 31, 1992
- Incomplete Griffiths Scales of Mental Development at 18 months
- Incomplete information regarding alcohol consumption and alcohol binges during the postpartum period
- Incomplete information on the length of lactation and timing of supplementation in the first 3 months after birth
- Mothers enrolled after the end of the sixth month of pregnancy
- Birth not a singleton and less than 34 weeks gestation
- Down syndrome

Description of Study Protocol:

Recruitment

- This study used a subset of a larger study called The Avon Longitudinal Study of Parents and Children (ALSPAC) Study
- The ALSPAC is part of a series of studies conducted in Europe supported by the World Health Organization
- All women who reside in a defined area of Avon County, United Kingdom who had an expected delivery date of April 1, 1991 to December 31, 1992
- 10% of the ALSPAC participants were randomly selected for more intensive assessment, forming the Children in Focus cohort

Design

• Retrospective Cohort Study

Statistical Analysis

- Griffiths Scales of Motor development and the infant alcohol exposure via breast milk (IAA) were compared with each of the secondary variables
 - Gender, gestational age at birth and the psychometrist were adjusted for
 - Analysis of variance (generalized linear models), Kruskal-Wallis test and Spearman correlations were completed
 - If a variable had an association with both the IAA and at least one Griffiths scale with $P \le 0.15$, it was included in the regression of IAA on the primary outcome of motor development
- Griffiths Scales of Motor development and the infant binge variable were compared with each of the secondary variables
 - Gender, gestational age at birth and the psychometrist were adjusted for
 - Analysis of variance (generalized linear models), Kruskal-Wallis test and Spearman correlations were completed
 - If a variable had an association with both the IAA and at least one Griffiths scale with $P \le 0.15$, it was included in the regression of IAA on the primary outcome of motor development
- IAA in the highest and lowest quartile for each of the adjusted Griffiths scales were compared
- Duplicate analyses were also completed for the exclusive breastfeeders and the partial breastfeeders
- Searches for possible interactions between IAA and Griffiths scales by breastfeeding status were completed
- Outliers were examined during the analysis
- Statistically significant results were considered $P \le 0.05$.

Data Collection Summary:

Timing of Measurements

- Maternal maternal questionnaires completed at 18 and 32 weeks of pregnancy and 8 weeks after delivery provided information on:
 - Alcohol consumption during pregnancy and lactation
 - Demographics
 - Lifestyle information
- Food frequency questionnaire at 32 weeks gestation
- Questionnaire on lactation history at 4 weeks and 6 months after delivery
- Griffiths Scales of Mental Development administered at 18 months ±2 weeks of age
 - 10% of the children were evaluated later because of illness or other extenuating circumstances

Dependent Variables

- Griffiths Scales of Mental Development
 - 5 scales locomotor development, personal-social development, hearing and speech, hand and eye coordination and performance tests
 - General Intelligence Quotient (GQ) is the average of all scales
 - 8 trained psychometrists performed the assessments using the extended scales (0-8 years)
 - Each child was seen for approximately 45 minutes during a play session and was scored immediately afterwards
 - Interobservor consistency was addressed by tester observation and by repeatedly comparing each tester's scoring of a single assessment
 - Only year 2 scores are used in the study's analysis as the year 3 tests were not always completed due to time constraints

Independent Variables

- Alcohol intake
 - At 8 weeks postpartum questionnaire addressed usual drinking since delivery and binge drinking in the previous month
 - Questions were based on a serving of a standard-sized drinks that usually contain 0.5 fluid ounces of ethanol
 - A binge was considered 4 or more standard-size drinks on a single occasion
 - An average fluid ounces of absolute alcohol was estimated
- Infant Alcohol score (IAA): proxy variable for the amount of ethanol available to the infant via breast milk
 - obtained by multiplying the maternal AA score by the summary index of the infant's breastfeeding experience
 - similar indicator of infant exposure to nunmnber of binge days was also calculated.

Control Variables

- Nutrient intake
- Lactation and supplementation history
- Postpartum smoking and marijuana use
- Caffeine intake
- Parity
- Employment
- Housing situation
- Marital and cohabitation status

Description of Actual Data Sample:

Initial N:

• ALSPAC group: 10,000

• Children in Focus subset: 1,400

Attrition (final N):

• 915

Age:

• Under 20 years: 2.3%

20-29 years: 51%30-39 years: 45.1%40 or more: 1.5%

Ethnicity:

White: 97.7%Nonwhite: 2.3%

Other relevant demographics:

- Maternal education
 - No qualifications or vocational school: 21.4%
 - O level ("secondary school" completed): 36.1%
 - A level (college preparatory completed): 27.2%
 - College degree: 15.3%
- Parity
 - 1 child: 45.9%
 - 2-3 children: 48.7%
 - 4 or more children: 5.4%
- Married
 - Yes: 83.5%
 - No: 16.5%
- Employed
 - Yes: 50.1%
 - No: 49.9%
- Housing situation:
 - Owned/mortgaged: 83.3%
 - Public housing: 9.2%
 - Rented/other: 7.5%

Location: Avon County, United Kingdom

Summary of Results:

Key Findings

- The usual drinking patterns in the sample showed only 5% having 2 or more drinks a day during the postpartum period. Binges in the postpartum period were reported by 37% of all women.
- Three of the five Griffiths scales showed a signficant rise with increasing IAA.
- When infant exposure via binge was analyzed, only the average score showed the same positive association.
- Results were similar when restricted to exclusive breastfeeders, partial breast feeders, considered interaction by breastfeeding status, and compared the exposure of infants having the lowest and highest Griffiths scores.

Characteristics (N Valid Values; Percentage in Each Category Shown)	Average of All Scales	Hand-Eye Coordination	Hearing and Speech	Locomotor Scale	Social / Personal	Performance
Estimated infant exposure to alcohol in breast milk (oz/day) ^b						
None (295)	107.3	106.7	98.3**	111.9	103*	114.2*
>0 but <0.1 (295)	108.1	106.6	100.4	112.7	104.5	114.1
0.1-0.4 (257)	108.9	107.2	102.9	112.9	105.2	114.1
0.5-0.9 (51)	108.2	106.7	102	111.9	104.1	114.5
1 or more (17)	109.8	105.3	100.6	115.8	108.7	115.2
Estimated infant alcohol exposure via binge (binges per month)b						
0 (656)	107.7*	106.6	99.9	112.1	103.7	114
<0.5 (60)	108.9	105.6	101.9	114.2	105.6	113.1
0.5-0.9 (81)	108.4	107.6	101.4	113.2	104.3	113.4
1-1.9 (74)	110.7	108.6	103.8	114.6	106.8	117.2
2 or more (44)	108.1	106.2	101	111.8	105.1	113.7
Maternal education (906)						

No qualifications or vocation school (21.4%)	106***	104.9**	96.1***	113.2	103.9***	111.8***
Regular caffeine us during pregnancy (908)						
Yes (63.5%)	107.3**	106.3	99.7	111.5***	105.3**	113.6
No (47%)	108.8	107.3	101.2	113.5	107.3	114.7

 $[*]P \le 0.05, **P \le 0.01, ***P \le 0.001$

^aAll variables were considered in the adjustment. Only variables related to both infant alcohol and at least 1 Griffiths score were entered into the regression analysis

bInfant alcohol exposure is the absolute alcohol content of maternal alcohol intake on an average day multiplied by the proportion of breast milk in the infant's diet. This estimator includes the ethanol in binges. Infant alcohol exposure via binge is the product of the number of binges in the previous month and the proportion of breast milk in the diet.

Other Findings

Characteristics (N Valid Values; Percentage in Each Category Shown)	Average of All Scales	Hand-Eye Coordination	Hearing and Speech	Locomotor Scale	Social / Personal	Performance
Maternal education (906)						
No qualifications or vocation school (21.4%)	106***	104.9**	96.1***	113.2	103.9***	111.8***
O level ("secondary school completed) (36.1%)	108	107.1	100.2	112.4	106.7	113.5
A level (college preparatory completed) (27.2%)	108.5	107.1	101.6	112	106.7	115

College degree (15.3%)	110.3	108.3	105.3	112.6	107.8	117.3
Maternal age (915)						
Under 20 (2.3%)	104.6	104.5	94.2	112.4	100*	112.1
20-29 (51%)	108.1	106.7	100.6	112.6	106.4	113.8
30-39 (45.1%)	108.2	107	100.6	112.4	106.4	114.6
40 or more (1.5%)	106.1	104.6	97.9	108.5	103.4	115.6
Parity (905)						
1 (45.9%)	108.7***	106.4	103***	112.6	107.1***	114
2-3 (48.7%)	107.9	107.4	98.8	112.5	105.9	114.7
4 or more (5.4%)	104.2	104.3	92.9	110	101.9	111.5
Ethnicity (896)						
White (97.7%)	108	106.7	100.4	112.3*	106.2	114.1
Nonwhite (2.3%)	110.7	108.6	102.1	116.9	109.7	116.1
Married (905)						
Yes (83.5%)	108.3*	106.8	100.8	112.6	106.5*	114.5*
No (49.9%)	106.7	106.5	98.4	111.6	104.5	112.4
Employed (797)						
Yes (83.5%)	108.6*	106.5	101.8*	112.7	106.9*	115*
No (49.9%)	107.5	106.9	99.1	112.2	105.5	113.3
Housing Situation (909)						
Owned / mortgaged (83.3%)	108.3*	107	101.1**	112.4	106.6	114.5
Public housing (9.2%)	106.6	106.1	96.2	112.7	105.1	112.3
Rented / other (7.5%)	106.4	104.9	98.5	112.7	103.9	111.9
All infants (915)	108	106.8	100.4	112.4	106.2	114.2

Characteristics (N Valid Values; Percentage in Each Category Shown)	Average of All Scales	Hand-Eye Coordination	Hearing and Speech	Locomotor Scale	Social / Personal	Performance
Alcohol Use ^a (915)						
Average daily alcohol use postpartum (oz ethanol)						
None (16.6%)	107.3	107.5	96***	112.4	105.1*	115
>0 but <0.1 (29%)	107.6	106.3	99.9	112.1	106	113.7
0.1-0.4 (39.6%)	108.8	107	102.7	112.9	107.3	114.1
0.5-0.9 (9.7%)	107.6	106.7	100.9	111.3	104.3	114.8
1.0 or more (5.1%)	107.3	104.9	98.8	113.3	106.2	113.3
Binges postpartum (days in previous month)(915)						
None (62.6%)	107.8	106.6	100	111.9*	106.1	114.3
1-2 days (22.3%)	108.9	107.5	101.7	114	107.2	114
3-4 days (11.6%)	108.2	106.5	101.5	112.6	105.7	114.6
5 or more days (3.5%)	106.9	106	98.7	111.9	104.9	113
Average daily alcohol us, early in pregnancy (oz ethanol) (887)						
None (41%)	108.5	107.5	100.4	112.5	106.7	115.3*
>0 but <0.1 (34.3%)	107.1	105.7	99.5	111.7	105.8	112.8

0.1-0.4 (19.5%)	109	107.1	103.1	113.7	106.3	114.5
0.5-0.9 (3.2%)	107.4	107.4	98.3	111.1	106.6	113.3
1 or more (2%)	107.2	106.4	98.4	113.3	105.9	111.7
Average daily alcohol use, late pregnancy (oz ethanol) (887)						
None (43.1%)	107.8	106.6	98.9*	112.5	106.1	114.7
>0 but <0.1 (34.3%)	108.6	106.9	102.6	112.1	107	114.1
0.1-0.4 (20.1%)	107.7	106.3	101	112.1	105.3	113.8
0.5-0.9 (4.1%)	108.4	108.9	99.7	114	107.4	111.8
1 or more (1.7%)	108.3	108.3	97.5	116.4	105	114.1
Other drug use						
Smoker postpartum (909)						
Yes (15.2%)	107.4	106.7	98.4	113.8*	105.6*	111.9
No (84.8%)	108.1	106.8	100.8	112.1	106.3	114.6
Smoker during pregnancy (911)						
Yes (11.9%)	107	107.3	97.7*	112.7	105.5	111.8*
No (88.1%)	108.2	106.7	100.8	112.4	106.3	114.5
Regular caffeine us postpartum (816)						
Yes (63.5%)	108	107.2	100.1	112.4	106.1	114.3
No (36.5%)	108.1	106.3	100.7	112.4	106.7	114.3
Regular caffeine us during pregnancy (908)						
Yes (53%)	107.3**	106.3	99.7	111.5***	105.3**	113.6
No (47%)	108.8	107.3	101.2	113.5	107.3	114.7

Marijuana use postpartum (870)						
Yes (1.4%)	104.8	108.9	95.6	111.2	98.9**	109.1
No (98.6%)	108.1	106.7	100.6	112.5	106.3	114.2
Marijuana use during pregnancy (880)						
Yes (1.4%)	109.4	109.6	99.6	114.2	105.7	117.4
No (98.6%)	108	106.7	100.5	112.5	106.3	114.2
All infants (915)	108	106.8	100.4	112.4	106.2	114.2

^aUsual alcohol use is presented in average ounces of ethanol consumed per day. One standard size drink of any alcoholic beverage contains about 0.5 fl oz of ethanol

 $[*]P \le 0.05, **P \le 0.01, ***P \le 0.001$

Characteristics (N Valid Values; Percentage in Each Category Shown)	Average of All Scales	Hand-Eye Coordination	Hearing and Speech	Locomotor Scale	Social / Personal	Performance
Proportion of diet provided by breast milk for first 3 months (915)						
Exclusive bottle-feeding (19.8%)	105.8***	105.4	96.9**	111.2	103.3***	112*
Some breast, but under 50% (19.5%)	108	106.7	99.8	112.3	106.7	114.5
50% or more, but not exclusive breastfeeding (31.9%)	108.7	107.5	101.8	113	107	114.2

Exclusive breastfeeding (28.9%)	108.8	106.9	101.7	112.7	107	115.4
All infants (915)	108	106.8	100.4	112.4	106.2	114.2

 $[*]P \le 0.05, **P \le 0.01, ***P \le 0.001$

Adjusted Griffiths Scores by Infant Alcohol Exposure^a (915)

Characteristics (N Valid Values; Percentage in Each Category Shown)	Average of All Scales	Hand-Eye Coordination	Hearing and Speech	Locomotor Scale	Social / Personal	Performance
Estimated infant exposure to alcohol in breast milk (oz/day) ^b						
None (295)	107.3	106.7	98.3**	111.9	103*	114.2*
>0 but <0.1 (295)	108.1	106.6	100.4	112.7	104.5	114.1
0.1-0.4 (257)	108.9	107.2	102.9	112.9	105.2	114.1
0.5-0.9 (51)	108.2	106.7	102	111.9	104.1	114.5
1 or more (17)	109.8	105.3	100.6	115.8	108.7	115.2
Estimated infant alcohol exposure via binge (binges per month)b						
0 (656)	107.7*	106.6	99.9	112.1	103.7	114
<0.5 (60)	108.9	105.6	101.9	114.2	105.6	113.1
0.5-0.9 (81)	108.4	107.6	101.4	113.2	104.3	113.4
1-1.9 (74)	110.7	108.6	103.8	114.6	106.8	117.2
2 or more (44)	108.1	106.2	101	111.8	105.1	113.7

* $P \le 0.05$, ** $P \le 0.01$, *** $P \le 0.001$ for significance of F value in generalized linear models analysis

^aAll variables were considered in the adjustment. Only variables related to both infant alcohol and at least 1 Griffiths score were entered into the regression analysis

^bInfant alcohol exposure is the absolute alcohol content of maternal alcohol intake on an average day multiplied by the proportion of breast milk in the infant's diet. This estimator includes the ethanol in binges. Infant alcohol exposure via binge is the product of the number of binges in the previous month and the proportion of breast milk in the diet.

Thiamin, niacin, Vitamin B6, Vitamin C, folate, magnesium, soluble fiber and total iron had Spearman correlation coefficients of ≤ 0.2 for infant alcohol exposure and ≤ 0.1 for the developmental scales (data not provided).

Author Conclusion:

Infant motor development was not adversely associated by infant exposure to alcohol via breast milk. Several components of development were weakly but positively related to maternal drinking during lactation. The smaller effect of alcohol exposure in breast milk may require longer term studies where the children are tested at an older age to detect significant effects.

Reviewer Comments:

This authors do not provide any theories as to why three of the Griffiths scales increased significantly with increasing infant alcohol exposure.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

- 1. Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)
- 2. Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?
- 3. Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?
- 4. Is the intervention or procedure feasible? (NA for some epidemiological studies)

Validity Questions

1. Was the research question clearly stated?



N/A

	1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
	1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
	1.3.	Were the target population and setting specified?	Yes
2.	Was the sele	ection of study subjects/patients free from bias?	Yes
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
	2.2.	Were criteria applied equally to all study groups?	Yes
	2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study	groups comparable?	Yes
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method	of handling withdrawals described?	Yes
	4.1.	Were follow-up methods described and the same for all groups?	Yes
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes

	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
	4.4.	Were reasons for withdrawals similar across groups?	Yes
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blindin	g used to prevent introduction of bias?	Yes
	5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
	5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
	5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
	5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
	5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.		ention/therapeutic regimens/exposure factor or procedure and ison(s) described in detail? Were interveningfactors described?	Yes
	6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
	6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
	6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
	6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
	6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
	6.6.	Were extra or unplanned treatments described?	Yes
	6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
	6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcom	mes clearly defined and the measurements valid and reliable?	Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes

	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the stat	tistical analysis appropriate for the study design and type of licators?	Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	Are conclusions consideration	ions supported by results with biases and limitations taken into on?	Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due t	o study's funding or sponsorship unlikely?	Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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